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REVIEW

SUPERIOR VENA CAVA SYNDROME

Bianca Paraschiv[1,2], Giorgiana Dediu[1,2], Adela Iancu[3], Ovidiu Bratu[1,4], Camelia Diaconu[1,5]

[1] University of Medicine and Pharmacy „Carol Davila" Bucharest, Romania
[2] Clinical Emergency Hospital „Sf. Ioan", Bucharest, Romania
[3] Family Medicine Department, University of Medicine and Pharmacy „Carol Davila" Bucharest, Romania
[4] University Emergency Central Military Hospital „Dr. Carol Davila", Bucharest, Romania
[5] Clinical Emergency Hospital of Bucharest, Romania

Abstract

Superior vena cava syndrome (SVCS) is a medical condition which consists of the obstruction of blood flow through the superior vena cava. Congenital or acquired abnormalities can affect the diameter of SVC. The complete obstruction of SVC leads to SVCS. In the preantibiotic era, the untreated infections were the most frequent causes of the SVCS, but today malignancy is the most common etiology. Symptoms usually have a gradual onset and dyspnea remains the most important one. Conventional venography is the gold standard for identifying the location, the extent and the hemodynamic significance of the obstruction, being superior to CT scan, even though it can not demostrate the cause. The differential diagnosis includes pulmonary infections, cardiac tamponade, thoracic aortic aneurysm, chronic obstructive pulmonary disease. The treatment goals are to relieve the symptoms and to cure the underlying cause. The medical care includes anticoagulants, glucocorticoids, diuretics, as well as radio- and chemotherapy. The surgical approach involves stent placement and venous bypass. The prognosis depends entirely on the underlying disease.

Résumé

Le syndrome de la veine cave supérieure

Le syndrome de la veine cave supérieure (SVCS) est une affection médicale qui consiste en l›obstruction du flux sanguin à travers la veine cave supérieure. Des anomalies congénitales ou acquises peuvent affecter le diamètre du SVC. L›obstruction complète de SVC conduit à SVCS. Dans l›ère préantibiotique, l›infection non traitée était la cause la plus fréquente du SVCS, mais aujourd'hui la malignité est l›étiologie la plus fréquente. Les symptômes ont habituellement un début progressif et la dyspnée reste la plus importante. La Vénographie conventionnelle est l'étalon-d'or pour l'dentification de l›emplacement, l'étendue et la signification hémodynamique de l'obstruction, étant supérieure à la tomodensitométrie, même si elle ne peut pas démontrer la cause. Le diagnostic différentiel comprend les infections pulmonaires, la tamponnade cardiaque, l'anévrisme de l'aorte thoracique, la bronchopneumopathie chronique obstructive. Les objectifs du traitement sont de soulager les symptômes et de guérir la cause sous-jacente. Les soins médicaux comprennent les anticoagulants, les glucocorticoïdes, les diurétiques, comme la radio-et la chimiothérapie.

Correspondence address: Dr. Camelia Diaconu
Internal Medicine Clinic, Clinical Emergency Hospital, 8 Calea Floreasca, 014461, Bucharest, Romania
e-mail: drcameliadiaconu@gmail.com

Key words: superior vena cava, malignancy, stent.

L'approche chirurgicale implique la mise en place d'un stent et le pontage veineux. Le pronostic dépend entièrement de la maladie sous-jacente.

Mots-clés: veine cave supérieure, cancer, stent.

Introduction. Embryology and anatomy

The superior vena cava (SVC) is formed in the 5th week of fetal life. On the right side there is an anastomosis between proximal right anterior cardinal vein, right common cardinal vein and right horn of the venous sinus.On the left side, a part of the left anterior cardinal vein regresses to form the ligament of Marshall and another part forms the left superior intercostal vein and the adjacent left brachiocephalic vein.The posterior cardinal vein also regresses. The coronary sinus is formed from the left horn of the sinus venosus[1]. The SVC is formed by the confluence of the right and left brachiocephalic veins. It is located on the right side of the middle mediastinum and is surrounded by sternum, trachea, right bronchus, aorta, pulmonary artery, and the perihilar and paratracheal lymph nodes.The SVC is the major drainage vessel for venous blood from the head, neck, arms, and upper torso. SVC has a length of 7.1±1.4 cm, and its maximum diameter in adults is 2.1±0.7 cm; it is a thin-walled, low-pressure, vascular structure[2].

Pathophysiology

No matter the etiology, if SVC is obstructed, the venous pressure in collateral vessels increases and, in time, a collateral blood-flow network will develop[3,4]. The most important pathway is the azygos vein, the hemiazygos vein, and the connecting intercostal veins. The second collateral network is the internal mammary venous system with its tributaries and the superior and inferior epigastric veins. The third pathway is represented by the long thoracic venous system. The fourth network consists of femoral veins and vertebral veins, which are connected with the long thoracic venous system.This large collateral network is usually developed in several weeks, especially if the obstruction occurred above the insertion of the azygos vein. So, if the SVC obstruction has a slow mechanism, the patients remain asymptomatic for a long period of time as the collateral network grows[4]. The obstruction of the SVC may be complete (as a result of intravascular thrombosis for example) or incomplete (due to extrinsec pressure)[3].

Definition

Superior vena cava syndrome (SVCS) is a medical emergency which consists of the obstruction of blood flow through the superior vena cava. It was first described by William Hunter in 1757, in a patient with a large syphilitic aortic aneurysm compressing the SVC[3,5].

Epidemiology

SVCS develops in about 5-10% of patients with a malignant intrathoracic lesion[6]. Right sided masses are more likely to cause SVCS, due to the anatomic location of the SVC. The diagnosis is made between the age of 40-60 years in the case of a malignant lesion and between the age of 30-40 years if a benign cause is identified[6]. The SVCS in children is usually secondary to congenital stenosis. The sex distribution is in favor of males, due to the high incidence of lung cancer in this population. The races distribution is influenced by the frequency of lung cancer and lymphomas in these populations[3,5].

Etiology

In the preantibiotic era, the untreated infections, such as tertiary syphilitic thoracic aortic aneurysms, or fibrosing mediastinitis, were the most frequent causes of the SVCS[3]. Nowadays, malignancy is the most common etiology of SVCS[3,4,7]. Benign causes, such as thrombosis due to catheters and pacemakers, now account for 20 – 40% of cases[7].

- *Lung cancer.* SVCS is more frequently associated with small cell lung cancer (SCLC) than with non small cell lung cancer (NSCLC), mainly because SCLC has a more central development. But because of a higher incidence, NSCLC is considered the main cause of SVCS[8]. The mechanisms are: extrinsec compression (by either primary tumor or lymph nodes) or direct tumor invasion[5,9,10,11].
- *Lymphoma.* SVCS is rarely seen in patients with Hodgkin lymphoma, despite its frequent presentation with mediastinal lymphadenopathy[5]. The most common subtypes of non-Hodgkin lymphoma associated with SVCS are: primary mediastinal large B-cell lymphoma with sclerosis, diffuse large cell and lymphoblastic lymphomas. The

mechanisms are the same: extrinsic compression (due to enlarged lymph nodes) and intravascular occlusion (in angiotropic lymphoma)[12].

- *Other malignant tumors*: thymic neoplasms, primary mediastinal germ cell neoplasms, mesothelioma, mediastinal lymph node metastases of solid tumors[3,5].
- *Thrombosis* may be related with central vein catheters and pacemakers.
- *Mediastinal fibrosis.*
- *Vascular disease*: aortic aneurysm, vasculitis, arteriovenous fistulas.
- *Infections*: syphilis, tuberculosis, histoplasmosis, blastomycosis, actinomycosis. The mechanisms are: fibrosing mediastinitis or contiguous spread from a pulmonary, pleural, or cutaneous infection as in nocardiosis[5].
- *Benign mediastinal tumors*: teratoma, cystic hygroma, thymoma, dermoid cyst.
- *Cardiac causes*: pericarditis, atrial myxoma.
- *Postradiation fibrosis.*

Clinical presentation

Symptoms usually have a gradual onset, the patient may be asymptomatic early in the clinical course of SVCS. As the obstruction of SVC advances, dyspnea is the main symptom. Other signs and symptoms include: neck swelling, swelling of the trunk and/or upper extremities, facial swelling, hoarseness, stridorchest pain, cough, dilated chest vein collaterals, weight loss, jugular venous distension, phrenic nerve paresis, plethora and dysphagia. Rarely, there have been reported hoarseness, headache, confusion, dizziness, night sweats, hypoxia, hyponatremia, and syncope[3,5,7]. The physical findings consist of distention of the neck and upper torso, facial edema, plethora, cyanosis, stupor, and even coma. In order to assess the clinical status and the treatment choice, several scores are used, which divide SVCS in life-threatening and nonlife- threatening[13,14]. The complications of SVCS may be: laryngeal edema, cerebral edema, decreased cardiac output and secondary hypotension, pulmonary embolism in the presence of a thrombus, local irritation or thrombosis of veins in the upper extremities, or delayed absorption of drugs from the surrounding tissues[3].

Paraclinical investigations

The role of imaging investigations is to identify the indirect signs of SVC dilatation and its probable cause[3].

- *Conventional venography*. It is considered the gold standard for identification of SVC obstruction. It involves the uniplanar or biplanar superior vena cavograms. This method has the advantage of identifying the location, the extent and the hemodynamic significance of the lesion, being superior to CT scan. It also plays a key role in planning stent placement. However it does not demonstrate the cause of the obstruction, unless it involves thrombotic material[2,15].
- *Chest X-Ray*. Since cancer is the most common underlying disorder, usually there are changes on the chest X-ray secondary to malignancies. A widening of the upper mediastinum or a round or oval opacity at the right tracheobronchial angle may suggest a SVC dilatation or an azygos vein dilatation[2,5].
- *Computed tomography scan with contrast*. This is the most accurate in identifying the collateral vessels, the extent of venous blockage, the SVC diameter and the underlying cause. It also shows the position of the central catheter if present, or calcifications along the SVC as a sign of calcified thrombi, fibrin sheaths, or implantable cardio-defibrillator lead fragments[2,16].
- *Magnetic resonance venography*. It has the same specificity with conventional venography in evaluating central venous obstruction. This procedure is usually used in patients with chronic renal failure or contrast dye allergies[2,17].
- *Doppler ultrasound*. Its role is to identify a thrombus in the subclavian, axillary and brachiocephalic veins. This method can identify indirect signs, as monophasic waveforms or lack of normal respiratory phasicity in the brachiocephalic, internal jugular, or subclavian veins[2].
- *Histologic diagnosis*. Some invasive procedures may be needed in order to confirm the malignant cause of SVCS: bronchoscopy, mediastinoscopy, video-assisted thoracoscopy, thoracotomy, bone marrow biopsies[5,18].

Differential diagnosis

Based on clinical status and paraclinical results, the differential diagnosis of SVCS includes: pneumonia (bacterial, viral or fungal), tuberculosis, chronic obstructive pulmonary disease, acute respiratory distress syndrome, mediastinitis, syphilis, cardiac tamponade, thoracic aortic aneurysm.

Treatment

The objectives of the management are to alleviate symptoms and cure the underlying cause. Initial approach should be guided by the severity of SVCS, such as brain edema, decreased cardiac output, or upper airway edema. In case of a malignant cause,

the anticipated response to specific treatment should also be considered[19]. The medical care includes anticoagulants, glucocorticoids, diuretics, as well as radio- and chemotherapy. The surgical approach involves endovascular treatment and venous bypass[20,21]. Endovascular treatment consists of stenting, percutaneous transluminal angioplasty (PTA) or thrombolytic therapy[22,23]. Current guidelines highlight the importance of an accurate histological diagnosis prior to treatment initiation[21]. Furthermore, in patients with central airway obstruction or severe laryngeal edema or cerebral edema, immediate treatment with stent placement followed by radiotherapy is required[3,20,21]. Carefully monitoring of patient's symptoms and the adverse effects of the administered treatment should be done on a long term.

- *Conservative treatment*. The goal is to reduce hydrostatic pressure: seated position, elevation of the head of the bed, oxygen therapy, fluid restrictions, antiemetics[5].
- *Antibiotics*. In the presence of an infectious etiology, antibiotics are the first line of treatment[24,25].
- *Anticoagulants*. In the presence of a thrombus around a central catheter, treatment consists of: removal of the catheter combined with anticoagulation. The anticoagulation may be done using thrombolytics (streptokinase, urokinase, recombinant tissue-type plasminogen activator) or anticoagulants (heparin) or oral anticoagulants).The anticoagulation should be initiated in the first five days after the onset of symptoms and continued indefinitely[22].
- *Glucocorticoids*. The administration of glucocorticoids is recommended in the presence of a laryngeal edema, in patients undergoing radiotherapy, and in reversing symptoms caused by malignancies such as lymphoma or thymoma. The duration of administration should be short, with slowly decreasing dose[4,23].
- *Diuretics*. They are recommended with the hope that venous pressures distal to the obstruction may be affected by small changes in right atrial pressure[4,5].
- *Radiotherapy (RT).* It is used especially in patients with radiosensitive tumors. Although RT alone does not achieve complete control of SVC obstruction, it remains an important part of the SVCS management[26]. A temporary clinical response may be achieved in first 72 hours, but 20% of patients remain symptomatic[5]. The radiotherapy may be: palliative (3–4 Gy for the first 2–5 fractions, followed by 2 Gy fractionation to a total dose of 30–50 Gy), definitive (3–4 Gy for first 2–3 days, followed by fractionation of 1.8–2 Gy/day)[4]. The radiation field should include a 2 cm margin around the tumor[27].
- *Chemotherapy (CT).*It is indicated in patients with chemosensitive tumors (small cell lung cancer, non-Hodgkin lymphoma). The relief of the symptoms occurs in one to two weeks and long-term remission and durable palliations are achieved[8]. The administration can be by the dorsal foot vein[5]. In specific cases, RT may be added to CT, in order to obtain a better control of the malignancy and improve overall survival.
- *Surgical bypass*. This procedure is reserved for patients with severe persistent symptoms after endovenous treatment or in case of resistent carcinoma to CT and RT. There is no guideline regarding the optimal technique[28]. It is most often performed in the presence of mediastinal fibrosis.
- *Stent placement*. It is indicated even before a histological diagnosis is available, in patients who require urgent treatment: severe symptoms such as stridor, especially in non-small cell lung cancer, mesothelioma and recurrent disease after RT and CT. The symptoms' relief is obtained rapidly: headache immediately after the procedure, facial edema within 24 h, and upper extremity and truncal edema up to 72 h[4]. No matter the type of stent used (Gianturco Z stent, the Palmaz stent, the Wallstent, self-expanding stents), the reports show a rate of success in malignancy cases of 95-100%, with a rate of relapse of 0-40%[5]. Through a guide wire, one or more stents are placed percutaneously via the internal jugular, subclavian, or femoral vein, using a local anesthetic at the venous access site. The presence of a thrombotic occlusion is not a contraindication; in this case, an initial angioplasty to pre-dilate the SVC is necessary. Because there are no guidelines regarding the role of thrombolytic therapy associated with stent placement, several studies suggest different approaches: in case of a thrombus, pharmacologic thrombolysis or mechanical thrombectomy (with the risk of increased bleeding); to prevent reocclusion, anticoagulation for one to nine months or antiplatelet therapy, alone or dual antiplatelet therapy for 4-12 weeks[5]. The procedure may be associated in 3-7% of the cases with minor complications (infection, hematoma at the insertion site) and major complications (pulmonary embolism, pulmonary edema, pericardial tamponade, stent migration, bleeding, perforation or rupture of the stent, reocclusion and death)[4,5].

Prognosis

Survival in patients with SVCS is influenced by the underlying disease. In patients with benign etiology, life expectancy remains the same. If there is a malignant cause associated with SVCS, there is an average life expectancy of 6 months, with an important variability depending on the histopathological type[5]. The survival in SVCS secondary to mediastinal fibrosis can

be up to 9 years[4]. Patients presenting laryngeal and cerebral edema have a high risk of sudden death. Patients who have potentially curable disease should benefit from all available therapies in order to obtain it.

Conclusions

The main etiology for the obstruction of the blood flow in the SVC is malignancy[29]. Approximately 95% of tumors are lung cancer or non-Hodgkin lymphoma[5]. Current management guidelines highlight the importance of histological diagnosis prior to starting therapy. For emergency situations, endovenous stenting followed by radiotherapy are recommended. Stenting is also recommended in patients in whom chemotherapy or radiation have failed. There are no randomized trials comparing the efficacy of endovenous stents versus palliative RT or systemic chemotherapy. In the presence of a thrombus, systemic anticoagulation should be considered to limit extension of thrombus. Proper anticoagulation/antiplatelet therapy after stent placement haven't been yet established by the guidelines; however, the general consent suggests a three-months course of dual antiplatelet therapy. The prognosis depends entirely on the underlying disease.

References

1. HS Baldwin, E Dees. Embryology and physiology of the cardiovascular system. In: Gleason CA, Juul SE, eds. Avery's diseases of the newborn. 9th ed. Philadelphia, Pa: Saunders, 2012; 699–713.
2. SK Sonavane, DM Milner, SP Singh, AKA Aal, KS Shahir, A Chaturvedi. Comprehensive imaging review of the superior vena cava. *RadioGraphics* 2015; 35:1873–1892.
3. http://www.cancer.net. Accessed February 2017.
4. C Straka, J Ying, FM Kong, CD Willey, J Kaminski, DWN Kim. Review of evolving etiologies,implications and treatment strategies for the superior vena cava syndrome. *SpringerPlus* 2016; 5:229.
5. RE Drews, DJ Rabkin. Malignancy-related superior vena cava syndrome. www.uptodate.com. Accessed January 2017.
6. J Flounders. Superior vena cava syndrome. *Oncol Nurs Forum*. 2003;30(4):E84-88.
7. TW Rice, RM Rodriguez, RW Light. The superior vena cava syndrome: clinical characteristics and evolving etiology. *Medicine* 2006; 85:37.
8. NP Rowell, FV Gleeson. Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus: a systematic review. *Clin Oncol (R Coll Radiol)* 2002; 14:338.
9. C Diaconu, A Bălăceanu, M Ghinescu. A neck mass that dissapears at compression: is it a reason for concern? *Acta Medica Mediterranea* 2015, 31:339-341.
10. C Diaconu, B Paraschiv, R Lungu, D Bartoș. A rare cause of respiratory insufficiency: case presentation. *Central European Journal of Medicine* 2014;9(1):141-143.
11. B Paraschiv, C Ionescu, C Diaconu. Asymptomatic gigantic lung tumor: case report. *Medicine in Evolution* 2016, vol. XXII, 1:33-36.
12. DM Savarese, M Zavarin, MS Smyczynski, et al. Superior vena cava syndrome secondary to an angiotropic large cell lymphoma. *Cancer* 2000; 89:2515.
13. K Kishi, T Sonomura, K Mitsuzane, et al. Self-expandable metallic stent therapy for superior vena cava syndrome: clinical observations. *Radiology* 1993; 189:531–535.
14. JB Yu, LD Wilson, FC Detterbeck. Superior vena cava syndrome: a proposed classification system and algorithm for management. *J Thorac Oncol* 2008; 3:811–814.
15. R Uberoi. Quality assurance guidelines for superior vena cava stenting in malignant disease. *Cardiovasc Intervent Radiol* 2006; 29:319.
16. SD Qanadli, M El Hajjam, F Bruckert, et al. Helical CT phlebography of the superior vena cava: diagnosis and evaluation of venous obstruction. *AJR Am J Roentgenol* 1999; 172:1327.
17. J Lin, KR Zhou, ZW Chen, et al. Vena cava 3D contrast-enhanced MR venography: a pictorial review. *Cardiovasc Intervent Radiol* 2005; 28:795.
18. D Călina, L Roșu, AF Roșu, et al. Etiological diagnosis and pharmacotherapeutic management of parapneumonic pleurisy. *Farmacia* 2016;64 (6):946-952.
19. B Paraschiv, C Diaconu, S Dumitrache-Rujinski, et al. Treatment options in stage III non-small cell lung cancer. *Pneumologia* 2016;65(2):67-70.
20. PA Kvale, PA Selecky, UB Prakash. American College of Chest Physicians. Palliative care in lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007;132:368S.
21. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp (Accessed on February 2017).
22. CA Sirbu, E Furdu-Lungut, CF Plesa, CM Dragoi. Pharmacological treatment of relapsing remitting multiple sclerosis – where are we? *Farmacia* 2016;64(5):651-655.
23. AL Arsene, V Uivarosi, N Mitrea, CM Dragoi, AC Nicolae. *In vitro* studies regarding the interactions of some novel ruthenium (III) complexes withdouble stranded calf thymus deoxyribonucleic acid (DNA). *Farmacia* 2016;64(5):712-716.
24. D Călina, AO Docea, L Rosu, et al. Antimicrobial resistance development following surgical site infections. *Molecular medicine reports* 2016; 15: 681-688.
25. GTA Burcea-Dragomiroiu, DE Popa, BS Velescu, et al. Synthesis, characterization and microbiological activity evaluation of novel hard gelatine capsules with cefaclor and piroxicam, *Farmacia* 2016; 64 (6): 887-895.
26. S Cheng. Superior vena cava syndrome: a contemporary review of a historic disease. *Cardiol Rev* 2009:17:16–23.
27. S Mose, C Stabik, K Eberlein, et al. Retrospective analysis of the superior vena cava syndrome in irradiated cancer patients. *Anticancer Res* 2006; 26:4933.
28. GS Sfyroeras , CN Antonopoulos , G Mantas , et al. A review of open and endovascular treatment of superior vena cava syndrome of benign aetiology. *Eur J Vasc Endovasc Surg.* 2017;53(2):238-254.
29. B Paraschiv, C Diaconu, C Toma, M Bogdan. Paraneoplastic syndromes: the way to an early diagnosis of lung cancer. *Pneumologia* 2015;64(2):14-19.